

133
Sub
D1
phenylthiomethyl, (2-methoxy)phenylthiomethyl, benzylthiomethyl, (pyrid-2-yl)thiomethyl, (pyrid-2-yl)methylthiomethyl, (5-methylisoxazol-3-yl)thiomethyl, (5-methylisoxazol-3-yl)methylthiomethyl, 2-benzylthio-2-methylethyl, 2(pyrid-2-yl)methylthio-2-methyl-ethyl, 2-(1-methyl-1H-imidazol-2-yl)methylthio-2-methylethyl, 2-(1-benzyl-1H-imidazol-2-yl)methylthio-2-methylethyl, or 2-(5-methylisoxazol-3-yl)methylthio-2-methylethyl.

34. The compound of Claim 4, wherein Y is -OH.
35. (New) The compound of Claim 4, wherein Y is fluoro.
36. (New) The compound of Claim 4, wherein Y is NR₉R₁₀---

REMARKS

Claims 4, 6 and 20-36 are active. Claims 1-3, 5 and 7-19 have been withdrawn from consideration. As suggested by the Examiner, Claim 4 has been amended to incorporate the definitions of the R₁, R₂ and Y substituents of nonelected Claim 1. Support for the amendment of the last four lines of Claim 6 is found in the specification at page 4, lines 8-11 and page 2, line 24-page 3, line 10. New Claims 20-36 cover additional embodiments of the invention having particular classes or types of substituents, as described, for instance, on pages 2-9 of the specification. Particular R₁ substituents are described at page 8, lines 4-16. Particular R₂ substituents are described at page 8, line 17-page 9, line 20 and page 8, line 20-31. Accordingly, the Applicants do not believe that any new matter has been added.

RESTRICTION/ELECTION

The Applicants note that the restriction requirement has been made final.

PRIORITY

The Applicants thank the Examiner for acknowledging the priority claim under 119(e). If later required, the Applicants reserve the right to point out support within the provisional application for any pending claim.

REJECTION--35 U.S.C. 102

Claim 4 was rejected under 35 U.S.C. 102(b) as being anticipated by Boyle, et al., Chem. Abstract 119:240883. This rejection is moot in view of the amendment of Claim 4 to exclude the compound of Boyle et al. See the first proviso at the end of Claim 4.

REJECTION--35 U.S.C. 102

Claim 4 was rejected under 35 U.S.C. 102(b) as being anticipated by Griffith, et al., Chem. Abstract 108: 150945. This rejection is moot in view of the amendment of Claim 4 to exclude the compound of Griffith et al., see the second proviso of Claim 4.

REJECTION--35 U.S.C. 102

Claim 4 was rejected under 35 U.S.C. 102(b) as being anticipated by Freskos et al., Chem. Abstract 129: 244921. This rejection is moot in view of the amendment of Claim 4 to exclude the compound of Freskos et al., see the last proviso.

REJECTION--35 U.S.C. 103

Claims 4 and 6 were rejected under 35 U.S.C. 103(a) as being unpatentable over Bender et al., EP 0780386. Bender does not render the claimed compounds obvious, because this document does not disclose or suggest the compounds of the present invention. The

rejection indicates that Bender generically embraces the compounds of the invention when in formula (I) on page 4 of Bender, Y is hydroxy, R¹ (which partially corresponds to R₂ of the invention) is lower alkyl and R² (which partially corresponds to Y of the invention) is NR⁶R⁷ (which partially corresponds to NR₉R₁₀ of the invention). However, R² in the present invention is not lower alkyl, when Y is NR₉R₁₀, see proviso a) in Claim 4 of this amendment (page 5, line 2). Thus, Bender does not generally embrace the compound of the present invention, where the R₂ and Y groups are not simultaneously lower alkyl and NR⁹R¹⁰. Moreover, there is no suggestion in Bender for compounds where R₂ and Y groups are not simultaneously lower alkyl and NR₉R₁₀. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

The Applicants respectfully submit that this application is now in condition for allowance, in view of the above amendments and remarks. Early notification to that effect is earnestly solicited.

Respectfully submitted,

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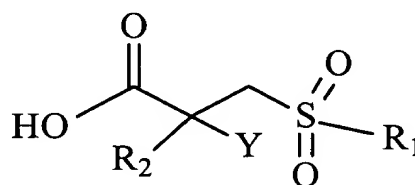
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MARKED-UP COPY OF AMENDMENT

IN THE CLAIMS

Please amend Claims 4 and 6 as follows:

--4. (Amended) A compound formula 8:



or a pharmaceutically acceptable salt[s] thereof,

wherein [R₁, R₂ and Y are as defined in claim 1]

R₁ is

a) C₄₋₁₂ alkyl,

b) C₄₋₁₂ alkenyl,

c) C₄₋₁₂ alkynyl,

d) -(CH₂)_h-C₃₋₈ cycloalkyl,

e) -(CH₂)_h-aryl,

f) -(CH₂)_h-het,

R₂ is

a) C₁₋₁₂ alkyl,

b) C₂₋₁₂ alkenyl,

c) C₂₋₁₂ alkynyl,

d) -(CH₂)_h-C₃₋₈ cycloalkyl,

e) $-(CH_2)_h-C_{3-8}$ cycloalkenyl,

f) $-(CH_2)_h$ -aryl,

g) $-(CH_2)_h$ -het,

h) $-(CH_2)_h$ -O,

i) $-(CH_2)_i$ -Q or $-(CH_2)_i$ -X-R₄, optionally the $-(CH_2)_i$ - chain can be substituted

with one or two C₁₋₄ alkyl or phenyl, which in turn can be substituted with one to three halo or

C₁₋₄ alkyl, or

l) $-(CH_2)_h$ CHR₅R₆;

R₃ is

a) H,

b) C₃₋₆ cycloalkyl,

c) C₁₋₄ alkyl, or

d) $-(CH_2)_h$ -phenyl;

X is

a) -O-

b) -S(=O)_j-;

c) -NR₇-;

d) -S(=O)₂NR₈-; or

e) -C(=O)-;

R₄ is

a) H,

b) C₁₋₈ alkyl,

c) $-(CH_2)_h$ -phenyl, or

d) $-(CH_2)_h$ -het;

R₅ is

a) C₁₋₄ alkyl, or

b) -C(=O)R₃;

R₆ is

a) -C(=O)R₃, or

b) -(CH₂)_nC(=O)R₃;

R₇ is

a) H,

b) C₁₋₄ alkyl,

c) -(CH₂)_n-phenyl,

d) -C(=O)-R₃,

e) -S(=O)₂R₃, or

f) -C(=O)OR₃;

R₈ is

a) C₁₋₄ alkyl, or

b) -(CH₂)_n-phenyl;

Y is

a) -OH,

b) -NR₉R₁₀, or

c) fluoro;

R₉ and R₁₀ are the same or different and are

a) H,

b) -C(=O)-R₃,

c) -C(=O)-OR₃, or

d) -C(=O)-NHR₃;

aryl is monocarbocyclic, or a bicarbocyclic aromatic moiety;

het is a 5- to 10-membered unsaturated monocyclic or a bicyclic heterocyclic moiety
having one to three atoms selected from the group consisting of oxygen, nitrogen, and sulfur;

Q is a 5- to 10-membered saturated monocyclic or bicyclic heterocyclic moiety having
one to two atom(s) selected from the group consisting of oxygen, nitrogen, and sulfur;

aryl, het, C₁₋₁₂ alkyl, C₁₋₄ alkyl, C₂₋₁₂ alkenyl, C₂₋₁₂ alkynyl, -C₃₋₈ cycloalkyl, -C₃₋₈
cycloalkenyl, Q and phenyl are optionally substituted;

h is 0, 1, 2, 3, 4, 5, or 6;

i is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

j is 0, 1, or 2;

with the following provisos:

a) where R₂ is C₁₋₆ alkyl, Y is other than -NR₉R₁₀;

b) where h is 0, het is attached to the α-position via the carbon atom of heterocyclic
moiety, and

c) where h is 0, Q is attached to the α-position via the carbon atom of heterocyclic
moiety;

wherein when Y is -OH and R₁ is phenyl substituted with fluorine, then R₂ is not C₁₋₂
alkyl,

wherein when Y is NH₂ and R₁ is -CH₂-phenyl, then R₂ is not C₁₋₂ alkyl, and

wherein when Y is -OH and R₁ is substituted phenyl, then R₂ is not C₁₋₂ alkyl.

6. [A] The compound of claim 4 [which] that is:

2-Hydroxy-2-(1-butylhydantoin-3-yl)methyl-3-(4-butoxybenzenesulfonyl)propionic acid;

2-Hydroxy-2-(1,5,5-trimethylhydantoin-3-yl)methyl-3-(4-butoxybenzenesulfonyl)propionic acid;

2-Hydroxy-2-(phenylthio)methyl-3-(4-butoxybenzenesulfonyl)propionic acid;

2-Hydroxy-2-(benzylthio)methyl-3-(4-butoxybenzenesulfonyl)propionic acid;

2-Hydroxy-2-(2-benzylthio-2-methylethyl)-3-(4-butoxybenzenesulfonyl)-propionic acid;

2-Hydroxy-2-(1-methylhydantoin-3-yl)methyl-3-(4-chlorobiphenylsulfonyl)propionic acid;

2-Hydroxy-2-(1-butylhydantoin-3-yl)methyl-3-(4-chlorobiphenylsulfonyl)-propionic acid;

2-Hydroxy-2-(1, 5, 5-trimethylhydantoin-3-yl)methyl-3-(4-chlorobiphenylsulfonyl)propionic acid;

2-Hydroxy-2-(phenylthio)methyl-3-(4-chlorobiphenylsulfonyl)propionic acid;

2-Hydroxy-2-(benzylthio)methyl-3-(4-chlorobiphenylsulfonyl)propionic acid;

2-Hydroxy-2-(pyrid-2-yl)thiomethyl-3-(4-chlorobiphenylsulfonyl)propionic acid;

2-Hydroxy-2-(5-methylisoxazol-3-yl)methylthiomethyl-3-(4-chlorobiphenylsulfonyl)propionic acid;

2-Hydroxy-2-[2-(1-methylhydantoin-3-yl)-2-methylethyl]-3-(4-chlorobiphenylsulfonyl)propionic acid;

2-Hydroxy-2-(2-benzylthio-2-methylethyl)-3-(4-chlorobiphenylsulfonyl)-propionic acid;

2-Hydroxy-2-(1-methylhydantoin-3-yl)methyl-3-(4-phenoxybenzenesulfonyl)propionic acid;

2-Hydroxy-2-(1-butylhydantoin-3-yl)methyl-3-(4-phenoxybenzenesulfonyl)propionic acid;

2-Hydroxy-2-(1, 5, 5-trimethylhydantoin-3-yl)methyl-3-(4-phenoxybenzenesulfonyl)propionic acid;

2-Hydroxy-2-(phenylthio)methyl-3-(4-phenoxybenzenesulfonyl)propionic acid;
 2-Hydroxy-2-(benzylthio)methyl-3-(4-phenoxybenzenesulfonyl)propionic acid;
 2-Hydroxy-2-[2-(1-methylhydantoin-3-yl)-2-methylethyl]-3-(4-phenoxy
 benzenesulfonyl)propionic acid;
 2-Hydroxy-2-[2-(1-methyl-1H-imidazol-2-yl)thio-2-methylethyl]-(4-phenoxy
 benzenesulfonyl)propionic acid;
 2-Hydroxy-2-(1,5,5-trimethylhydantoin-3-yl)methyl-3-[4-(pyrid-4-
 yl)benzenesulfonyl]propionic acid;
 2-Hydroxy-2-(phenylthio)methyl-3-[4-(pyrid-4-yl)benzenesulfonyl]propionic acid
 or
 2-Hydroxy-2-(1,5,5-trimethylhydantoin-3-yl)methyl-3-[4-(pyrid-4-yl)oxy
 benzenesulfonyl]propionic acid.--

Please add new Claims 20-36:

--20.-36. (New)--